UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,081	03/11/2004	Laurent Lecanu	1941.012US1	5330

21186 7590 03/07/2007

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,081	LECANU ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *5,19,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-18 and 20-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/10/05* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1 in the reply filed on July 20, 2006 and December 12, 2006 is acknowledged.

Applicant indicates that the traversal is on the ground(s) that the inventions are closely related. That is, the method of making the non-human animal (Group I) are related to the claims directed to methods of using the non human animal model (Group II) (Applicant's response, Applicant's emphasis, page 7, 2nd parag.). This is not found persuasive because while it has been acknowledged that there is a relationship between the two Inventions, the Restriction was applied because the searches are not necessarily coextensive. The claimed non-human animal can be used in other Applications, other than in a screen for agents that ameliorate symptoms for a neurologic disease. For example, the claimed non-human animal can be used to study the progression of disease. Applicant also indicates that the Restriction Requirement is traversed on the basis that Restrictions are optional in all cases. If the search and examination of at least a portion of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions (Applicant's response, page 7, 3rd parag. to page 8, 1st parag.). In response, this is not found persuasive because the Restriction was made based on the fact that the search and examination for the claimed invention was burdensome because the searches are not coextensive. That is, a search for the claimed non-human animal may provide a journal article discussing that

the non-human animal was used to characterize a disease; a search to determine whether that non-human animal was used to screen for agent that ameliorate symptoms of a disease would be another, independent search. Applicant indicates Applicant should not be required to incur the additional costs associated with the filing of a divisional application in order to obtain protection for the claimed subject matter (Applicant's response, page 8, 1st parag.). In response, issue of costs is not considered as a reason for withdrawing a restriction. Applicant indicates that Groups I and II can be searched efficiently and effectively in a single search as the Groups are in the same class (800). In response, a class search is not the only search that an Examiner performs. The searches include text-based searching, of which a search for the claimed non-human animal, in a screen for agents that treat a symptom, require additional search terms.

With regard to the election of a pro-oxidative compound, ferrous sulfate; an antioxidant inhibitor, buthionine sulfoximine; the pro-inflammatory compound, TNF-alpha (Applicant's response, July 20, 2006, page 8); Abeta compound, Abeta1-40; and phosphatase inhibitors, okadaic acid, (Applicant's response, December 12, 2006, page 7), Applicant indicates that the species election is traversed because the disclosed species have a disclosed relationship. That is, the disclosed species of Abeta compounds are Abeta compounds; the disclosed species of pro-oxidative compounds are pro-oxidative; the disclosed species of an antioxidant inhibitor is an antioxidant inhibitor; the disclosed species of a phosphatase inhibitor inhibit phosphatse, and the disclosed pro-inflammatory compounds are proinflammatory (Applicant's response, July

20, 2006, page 8, 3rd parag.). In response, the Examiner has considered Applicant's arguments persuasive and withdraws the restriction in part as it applies to the election of a pro-oxidative compound, an antioxidant inhibitor, a proinflammatory compound, and phosphatase inhibitors. With regard to the species election of an Abeta compound, the Examiner will consider Ab compounds that comprise Abeta42 (claim 2) and peptide fragments of Abeta42 (Abeta1-40 and Abeta24-35, claims 3 and 4). However, Abeta compounds that are peptidomimetics of Abeta42 remain restricted. The restriction remains because the search for peptidomimetics is burdensome because peptidomimetics are structurally different from peptides and require different search terms than that of peptides.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5, 19, 29, and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 20, 2006 and December 12, 2006.

Claims 1-4, 6-18, 20-28 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-18, 20-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at http://www.uspto.gov/web/menu/current.html#register).

The written description requirement for a claimed genus is satisfied by sufficient description of a representative number of species by actual reduction to practice and by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicant were in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

With regard to the claims being broadly drawn to the use of an "anti-oxidant inhibitor" the specification teaches that inhibitors of antioxidant defenses of the brain

that assist in triggering the physiolopathological modifications observed in human AD may include buthionine sulfoximine (BSO). Buthionine sulfoximine is an inhibitor of glutathion synthesis which may be used to lower the anti-oxidative defense of the brain (specification, page 8). While the specification provides this teaching, neither the art nor the specification provide structural guidance of other "anti-oxidant inhibitors" that are inhibitors of glutathion synthesis such that the genus of "anti-oxidant inhibitors" could be claimed. In addition to this, the art teaches that there are a variety of different kinds of antioxidants, including vitamin E, melatonin, estrogen, and superoxide dismutase (e.g. see Miranda et al., 2000, Progress in Neurobiology, 62: 633-648, abstract; and Schulz et al., 2000, European Journal of Biochemistry, 267: 4904-4911), each comprising very unique and distinct structures. Nothing in the specification or the art provides any structural guidance of any inhibitors of the antioxidants, listed above, nor is there a common "anti-oxidant inhibitor" which can be used to inhibit the activity of a variety of anti-oxidants. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision all the possible variant chemical structures used to arrive at an

anti-oxidant inhibitor, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only buthionine sulfoximine meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-4, 6-18, 20-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some

experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims broadly encompass any non-human animal. While the specification teaches that rats were used in the treatment to generate an animal model of disease (specification, page 13, table 1), the specification does not provide guidance that other animals can be used to arrive at the claimed invention. In addition to rats, the claimed invention includes animals such as flies, fish, and worms. However, post-filing art teaches that flies, fish, and worms are not good models of a brain disease because their brain anatomy is different from that of human and it is difficult to use these animals to address behavioral abnormalities (Gotz et al., 2004, Molecular Psychiatry, 9: 664-683, Figure 1). In addition to this issue, the art teaches that arriving at non-human

mammalian Alzheimer's models is unpredictable. Geula et al., 1998, Nature Medicine, 4: 827-831 teach that while injection of fibrillar Abeta into aged rhesus monkey cerebral cortex results in profound neuronal loss, tau phosphorylation, and microglial proliferation, injection into brains of aged marmoset monkeys is less toxic and is not significant in aged rats. Further, injection into young rhesus monkey cortex is not toxic (Geula et al., abstract). In another example, the Gotz et al., teach that when synthetic Abeta42 fibrils were injected in the hippocampus of transgenic mice that express wild type human tau, none of the mice exhibited any neurofibrillary tangles. This was surprising in light of the fact that Abeta was capable of forming tau filaments in a human tissue culture system. Gotz et al. teach that the inability to form tangles in mice reflects species differences between men and mice (Gotz et al., page 671, 2nd col., 2nd parag. under "Interaction of beta-amyloid and tau"). As these issues apply to the instant invention, while the specification teaches that rats were treated with iron, Abeta42, and buthionine sulfoximine (BSO) and exhibited phenotypes including amyloid plaques in their hippocampus, cingulate and temporal cortex (specification, page 15-16, parag. 49); neurofibrillary tangles (NFT) in their hippocampi (specification, page 16, parag. 50); latency in retrieving the platform in the Morris water maze (specification, page 15, parag. 49); vascular amyloidosis in the temporal cortex (specification, pages 16-17, parag. 51)and massive astrogliosis and microgliosis in the hippocampus (specification, page 17, parag. 52), the specification does not provide guidance that the method can be used to arrive at other non-human animal species encompassed by the claims. As such, the claims are limited to rat.

The claims broadly encompass any neurological disease. While the specification teaches a model of Alzheimer's disease, the specification does not provide guidance that the claimed non-human animal exhibits a wide variety of neurological diseases, as encompassed by the claims. These neurological diseases include amyotrophic lateral sclerosis (ALS), multiple sclerosis, and brain tumors. However, the specification does not provide guidance that the claimed non-human animal model exhibits any pathology or etiology related to these diseases and thus, the specification does not provide guidance to arrive at the full claimed scope. As such, the claims are limited to Alzheimer's disease.

The claims are broad for Abeta obtained from any species of animal. However, at the time of filing, the art teaches that potentiation of toxicity for mouse/rat Abeta1-40 is much less than that of human Abeta1-42 or Abeta1-40 (Huang et al., 1999, The Journal of Biological Chemistry, 274: 37111-37116, abstract). Huang et al. teach that rats and mice do not develop amyloid, even in transgenic mice that express endogenous mouse Abeta1-42. Huang et al. teach that this is likely due to three amino acid substitutions in the mouse homologue of Abeta (Huang et al., page 37111, 2nd col., 2nd parag.). As this issue applies to the instant invention, the claims are broadly drawn to use of Abeta from any species of animal; however, the art teaches that not all species of Abeta is able to produce amyloid. It is noted that while the specification teaches that Abeta42 was used to arrive at a rat that exhibited specific phenotypes, as described in the specification, pages 15-17, the specification does not provide guidance as to what species of animal Abeta42 was obtained from.

Thus, for these reasons, the claims are rejected.

Examiner's note: The claims appear to be free of art. It is noted that while the art teaches injection of iron and Abeta into rat cerebral cortex (e.g. Bishiop et al., 2002, Developmental Neuroscience, 24: 184-187) and neurons treated in vitro with zinc/copper, Abeta1-42, and BSO (Cuajungco et al., 2000, J. Biol. Chem, 275: 19439-19442), the art does not provide guidance to generate an animal model using all three compounds.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH